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STIC Database Tracking Number: 107753

To: Myron Hill **Location:** CM1/8A16/8E12 **Art Unit:** 1648 **Friday, November 07, 2003** **Case Serial Number:** 09/830981	**From:** Beverly Shears **Location:** Biotech-Chem Library CM1-1E05 **Phone:** 308-4994 **beverly.shears@uspto.gov**

Search Notes

Myron,

The attached table was used to identify hydrophilic/hydrophobic amino acids.

Beverly

Seq. Claim 1

FILE 'REGISTRY' ENTERED AT 11:19:04 ON 07 NOV 2003

L1 1588356 SEA ABB=ON PLU=ON [ACILMFPWYV][RNDQEHKST][RNDQEHKST][AC ILMFPWYV][2.][RNDQEHKST][ACILMFPWYV].[RNDQEHKST]/SQSP

L5 48470 S L1 AND SQL=<50

FILE 'HCAPLUS' ENTERED AT 11:28:36 ON 07 NOV 2003

L6 18205 S L5

L7 26 S L6 AND (CPP OR CELL PERMEAB?)

L7 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:396910 HCAPLUS

DOCUMENT NUMBER: 139:2887

TITLE: Design and pharmaceutical use of **cell-permeable** fusion peptides containing a protein transduction domain linked to the C-terminus of a Ras-like GTPase and inhibiting signaling by Ras-like GTPases

INVENTOR(S): Ten Klooster, Jean Pau; Van Hennik, Paula Baudewina; Voermans, Carlijn; Hordijk, Peter Lodewijk

PATENT ASSIGNEE(S): Stichting Sanquin Bloedvoorziening, Neth.

SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042239	A1	20030522	WO 2002-NL722	20021111

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-204305 A 20011112

AB The invention concerns a collection of **cell-permeable**, synthetic peptides that comprise a protein transduction domain (PTD), linked to the C-terminus of a Ras-like GTPase. These fusion peptides will enter eukaryotic cell (preferably mammalian cell) and will inhibit cellular functions, mediated by the GTPase of which the C-terminus was derived. Expts. using a set of these peptides encoding the C-termini of Rho-like GTPases show the potency and selectivity of inhibition, mediated by these peptides in a variety of primary and transformed human as well as rodent cell types. This invention will be useful to selectively interfere with signaling by Ras-like GTPases in vivo to counteract various types of human disease. A glycine residue may serve as a spacer in between the two domains. A spacer is not required, however. The amino acid sequences of PTDs that are preferably used

for the fusion peptides of this invention are disclosed. Use of the HIV-Tat PTD is most preferred. The present invention is applicable to all Ras-like GTPases, but those from the animal kingdom and particularly those from mammals are preferred, and most preferably those of human origin. The C-terminal peptides of the different GTPases that are included in this invention are defined as follows. Within the majority of Ras-like GTPases, various alpha helixes at homologous positions within the protein sequence can be identified. These helixes determine, in combination with a series of beta-sheets, the overall three-dimensional structure. In addition, a large number of Ras-like GTPases contain the CAAX-box or a similar motif at their C-terminal end. The peptides that are disclosed span the region from the first amino acid following the 5th and final alpha helix in the GTPase up until the amino acid directly preceding the cysteine residue of the CAAX box.

IT **528846-93-7P 528847-09-8P 528847-14-5P 528847-21-4P 528900-10-9P 528900-12-1P 528900-13-2P 528900-21-2P 528900-28-9P 528900-30-3P 528900-31-4P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-terminus, fusion peptide containing; design and pharmaceutical use of **cell-permeable** fusion peptides containing protein transduction domain linked to C-terminus of Ras-like GTPase and inhibiting signaling by Ras-like GTPases)

IT **227199-94-2P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PTD, fusion peptide containing; design and pharmaceutical use of **cell-permeable** fusion peptides containing protein transduction domain linked to C-terminus of Ras-like GTPase and inhibiting signaling by Ras-like GTPases)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:170594 HCAPLUS
DOCUMENT NUMBER: 138:338486
TITLE: Synthesis, Structure Elucidation, in Vitro Biological Activity, Toxicity, and Caco-2 **Cell Permeability** of Lipophilic Analogues of α-Conotoxin MII
AUTHOR(S): Blanchfield, Joanne T.; Dutton, Julie L.; Hogg, Ronald C.; Gallagher, Oliver P.; Craik, David J.; Jones, Alun; Adams, David J.; Lewis, Richard J.; Alewood, Paul F.; Toth, Istvan
CORPORATE SOURCE: School of Pharmacy, Institute for Molecular Bioscience and School of Biomedical Sciences, University of Queensland, Brisbane, 4072, Australia
SOURCE: Journal of Medicinal Chemistry (2003), 46(7), 1266-1272
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The α-conotoxin MII is a two disulfide bridge containing, 16 amino acid long peptide toxin isolated from the marine snail Conus magus. This toxin has been found to be a highly selective and potent inhibitor of neuronal nicotinic acetylcholine receptors (nAChRs) of the subtype α3β2. To improve the bioavailability of this peptide, two lipophilic analogs of MII have been synthesized, the first by coupling 2-amino-DL-dodecanoic acid (Laa) to the N terminus (LaaMII) and the second by replacing Asn5 in the MII sequence with this lipoamino acid (5LaaMII). Both lipophilic linear peptides were then oxidized under standard conditions. 1H NMR shift anal. of these peptides and comparison with the native MII peptide showed that the tertiary structure of the N-conjugated analog, LaaMII, was consistent with that of the native conotoxin, whereas the 5LaaMII analog formed the correct disulfide bridges but failed to adopt the native helical tertiary structure. The N terminus conjugate was also found to inhibit nAChRs of the subtype α3β2 with equal potency to the parent peptide, whereas the 5LaaMII analog showed no inhibitory activity. The active LaaMII analog was found to exhibit significantly improved permeability across Caco-2 cell monolayers compared to the native MII, and both peptides showed negligible toxicity.

IT **186420-62-2P**, α-Conotoxin M II (reduced)
478550-80-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminododecanoate and its incorporation into peptides as lipophilic analogs of α-conotoxin MII)

IT **175735-93-0P**, α-Conotoxin M II **478550-79-7P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, tertiary structure, nAChR inhibition, toxicity, and caco-2 **cell permeability** of lipophilic analogs of α-conotoxin MII)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:42362 HCAPLUS
DOCUMENT NUMBER: 138:103296
TITLE: Improvement of viral uptake into cells and tissues
INVENTOR(S): Sessa, William C.; Gratton, Jean-Philippe
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004600	A2	20030116	WO 2002-US20337	20020626

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-303117P P 20010705

AB The invention relates to compns. and methods for facilitating fusion of a virus with a cell and for facilitating virus-mediated transduction of a nucleic acid into a cell. The invention relates generally to compns. and methods for improving virus uptake into cells and tissues and for transducing nucleic acids into cells. The invention relates more specifically to compns. and methods for the use of **cell permeable** peptides to render cells susceptible to entry by viruses, which in turn improves expression of transduced nucleic acids at reduced titers of virus and increases the efficacy of therapeutically relevant nucleic acids in vivo.

IT **189036-95-1**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; improvement of viral uptake into cells and tissues)

L7 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:889628 HCAPLUS
DOCUMENT NUMBER: 138:137578
TITLE: Tandem Ligation of Multipartite Peptides with **Cell-Permeable** Activity
AUTHOR(S): Eom, Khee Dong; Miao, Zhenwei; Yang, Jin-Long; Tam, James P.
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University, Nashville, TN, 37232, USA
SOURCE: Journal of the American Chemical Society (2003), 125(1), 73-82
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper describes a tandem ligation strategy to prepare multipartite peptides with normal and branched architectures containing a novel transport sequence that is rich in arginine and proline, thus enabling **cell permeability**. This strategy consists of three ligation methods specific for amino terminal cysteine (Cys), serine/threonine (Ser/Thr), and Nα-chloroacetylated amine to afford Xaa-Cys, Xaa-OPro (oxaproline) and Xaa-ψGly (pseudoglycine) at the ligation sites, resp. Assembly of single-chain peptides from three different unprotected segments was achieved by the tandem Cys/OPro ligation to form two amide bonds, an Xaa-Cys and then an Xaa-OPro. Assembly of two- and three-chain peptides with branched architectures from four different segments was accomplished by tandem Cys/ψGly/OPro ligation. Without the need of a protection or deprotection step, these tandem ligation strategies were successful in generating **cell-permeable** multipartite peptides containing one-, two-, and three-chain architectures, ranging in size from 52 to 75 residues. The exptl. results show that there is considerable flexibility in

the architectural design to obtain **cell-permeable** multipartite peptides bearing a transport sequence.

IT **491599-66-7P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(tandem ligation between unprotected peptide segments for preparation of multipartite peptides with **cell permeability** and transport properties)

IT **489473-07-6P 491599-42-9P 491599-43-0P 491599-44-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tandem ligation between unprotected peptide segments for preparation of multipartite peptides with **cell permeability** and transport properties)

IT **491599-47-4P 491599-64-5P 491599-65-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(tandem ligation between unprotected peptide segments for preparation of multipartite peptides with **cell permeability** and transport properties)

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:692669 HCAPLUS
DOCUMENT NUMBER: 138:70348
TITLE: A novel class of **cell permeable** "karyophilic" peptides: NLS-mediated nuclear import of dermaseptin derived peptides in intact cells
AUTHOR(S): Hariton-Gazal, Elana; Gilon, Chaim; Mor, Amram; Loyter, Abraham
CORPORATE SOURCE: Department of Organic Chemistry, Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, 91904, Israel
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 959-960. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif. CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A peptide derived from the dermaseptin S4, called K4, was found to be non-karyophilic, which means that it only accumulated within the cell cytoplasm of intact cultured cells, although being of small mol. weight The penetration of K4 occurred at 37°C as well as at 4°C, indicating a non-metabolic dependent process. To determine whether the addition of NLS will confer karyophilic properties upon K4 while retaining its **cell permeability** properties, a composite peptides bearing both the sequence of the K4 peptide as well as the NLS motif of the SV4-T-antigen were synthesized. The various features that characterize nuclear import of the NLS-K4 composite peptides (PVK, KPV) were studied using an assay on digitonin-permeabilized cells. Similar to K4, the composite PVK and KPV peptides penetrated intact HeLa cells at

37°C as well as at 4°C. However, at 4°C these peptides were retained in the cytoplasm and did not accumulate within the intranuclear space. The import of PVK into nuclei of permeabilized HeLa cells was dependent on the addition of a reticulocyte extract indicating that its translocation, similar to the SV40-NLS conjugate, require cytosolic factors. In contrast to PVK, VPK peptide containing the reverse sequence of the SV40-NLS did not show any nuclear accumulation. This indicated that in permeabilized cells, nuclear import of the PVK and KPV was specific and mediated by a functional NLS.

IT **482371-25-5P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(KPV peptide; novel class of **cell permeable** "karyophilic" peptides and NLS-mediated nuclear import of dermaseptin derived peptides in intact cells)

IT **482371-24-4P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(PVK peptide; novel class of **cell permeable** "karyophilic" peptides and NLS-mediated nuclear import of dermaseptin derived peptides in intact cells)

IT **482371-23-3P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(RDK peptide; novel class of **cell permeable** "karyophilic" peptides and NLS-mediated nuclear import of dermaseptin derived peptides in intact cells)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:218605 HCAPLUS
DOCUMENT NUMBER: 136:382091
TITLE: Selective in vivo inhibition of mitogen-activated protein kinase activation using **cell-permeable** peptides
AUTHOR(S): Kelemen, Bradley R.; Hsiao, Kevin; Goueli, Said A.
CORPORATE SOURCE: Genencor International, Palo Alto, CA, 94304, USA
SOURCE: Journal of Biological Chemistry (2002), 277(10), 8741-8748
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The extracellular signal-regulated kinase (ERK), a member of the mitogen-activated protein kinases (MAPKs), is essential for cellular proliferation and differentiation, and thus there exists great interest to develop specific and selective inhibitors of this enzyme. Whereas small mol. inhibitors PD098095 and U0126 have been used to study MAPK/ERK kinase (MEK), their target selectivity has been questioned recently. The cross-reactivity of ATP-directed inhibitors with other protein kinases prompted us to develop

structure-based selective peptide inhibitors of ERK activation. Based on a MEK1-derived peptide, we developed inhibitors of ERK activation in vitro and in vivo. The inclusion of either an alkyl moiety or a membrane-translocating peptide sequence facilitated the cellular uptake of the peptide inhibitor and prevented ERK activation in 4-phorbol 12-myristate 13-acetate-stimulated NIH 3T3 cells or nerve growth factor-treated PC12 cells in a concentration-dependent manner. In addition, **cell-permeable** peptides inhibited ERK-mediated activation of the transcriptional activity of ELK1. The peptides did not have an inhibitory effect on the activity of two other closely related classes of MAPKs, c-Jun amino-terminal kinase or p38 protein kinase. Thus, these peptides may serve as valuable tools for investigating ERK activation and for selective investigation of ERK-mediated responses. With the knowledge of other kinase interacting domains, it would be possible to design **cell-permeable** inhibitors for investigating diverse cellular signaling mechanisms and for possible therapeutic applications.

IT **427884-67-1 427884-68-2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective in vivo inhibition of mitogen-activated protein kinase activation using **cell-permeable** peptides)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:128116 HCAPLUS
DOCUMENT NUMBER: 136:289341
TITLE: Y5 receptors mediate neuropeptide Y actions at excitatory synapses in area CA3 of the mouse hippocampus
AUTHOR(S): Guo, Hui; Castro, Peter A.; Palmiter, Richard D.; Baraban, Scott C.
CORPORATE SOURCE: Department of Neurological Surgery, University of California, San Francisco, CA, 94143, USA
SOURCE: Journal of Neurophysiology (2002), 87(1), 558-566
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuropeptide Y (NPY) is a potent modulator of excitatory synaptic transmission and limbic seizures. NPY is abundantly expressed in the dentate gyrus and is thought to modulate hippocampal excitability via activation of presynaptic Y2 receptors (Y2R). Here NPY, and commonly used Y2R-preferring (NPY13-36) and Y5 receptor (Y5R)-preferring ([D-Trp32]NPY and hPP) peptide agonists, evoke similar levels of inhibition at excitatory CA3 synapses in hippocampal slices from wild-type control mice (WT). In contrast, NPYergic inhibition of excitatory CA3 synaptic transmission is absent in mice lacking the Y5R subtype (Y5R KO). In both analyses of evoked population spike activity and spontaneous excitatory postsynaptic synaptic currents (EPSCs), NPY agonists induced powerful inhibitory effects in all hippocampal slices from WT mice, whereas these peptides had no effect in slices from Y5R KO mice. In slices from WT mice, NPY (and NPY receptor-preferring agonists) reduced the frequency of spontaneous EPSCs but had no effect on

sEPSC amplitude, rise time, or decay time. Furthermore, NPYergic modulation of spontaneous EPSCs in WT mice was mimicked by bath application of a novel Y5R-selective peptide agonist ([**cpp**]hPP) but not the selective Y2R agonist ([ahx5-24]NPY). In situ hybridization was used to confirm the presence of NPY, Y2, and Y5 mRNA in the hippocampus of WT mice and the absence of Y5R in knockout mice. These results suggest that the Y5 receptor subtype, previously believed to mediate food intake, plays a critical role in modulation of hippocampal excitatory transmission at the hilar-to-CA3 synapse in the mouse.

IT **118997-30-1**, Human peptide YY
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Y5 receptors mediation of neuropeptide Y actions at excitatory synapses in area CA3 of mouse hippocampus)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:48973 HCAPLUS
DOCUMENT NUMBER: 136:295079
TITLE: Antennapedia/HS1 chimeric phosphotyrosyl peptide: conformational properties, binding capability to c-Fgr SH2 domain and **cell permeability**
AUTHOR(S): Ruzza, Paolo; Donella-Deana, Arianna; Calderan, Andrea; Brunati, Annamaria; Massimino, Maria Lina; Elardo, Stefano; Mattiazzo, Alessio; Pinna, Lorenzo A.; Borin, Gianfranco
CORPORATE SOURCE: CNR-Biopolymers Research Center, Padua, 35131, Italy
SOURCE: Biopolymers (2001), 60(4), 290-306
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB With the aim of interfering with the signaling pathways mediated by the SH2 domains of Src-like tyrosine kinases, we synthesized a tyrosyl-phospho decapeptide, corresponding to the sequence 392-401 of HS1 protein, which inhibits the secondary phosphorylation of HS1 protein catalyzed by the Src-like kinases c-Fgr or Lyn. This phospho-peptide was modified to enter cells by coupling to the third helix of Antennapedia homeodomain, which is able to translocate across cell membranes. Here we present CD and fluorescence studies on the conformational behavior in membrane-mimicking environments and on lipid interactions of Antennapedia fragment and its chimeric phosphorylated and unphosphorylated derivs. These studies evidenced that electrostatic rather than amphiphilic interactions determine the peptide adsorption on lipids. Expts. performed with recombinant protein containing the SH2 domain of c-Fgr fused with GST and with isolated erythrocyte membranes demonstrated that the presence of the N-terminal Antennapedia fragment only slightly affects the binding of the phospho-HS1 peptide to the SH2 domain. In fact, it has been shown that in isolated erythrocyte membranes, both phospho-HS1 peptide and its chimeric derivative greatly affect either the SH2-mediated recruitment of the c-Fgr to the transmembrane protein band 3 and the following phosphorylation of the protein catalyzed by the Src-like kinase c-Fgr. The ability of the chimeric

phospho-peptide to enter cells has been demonstrated by confocal microscopy anal.

IT **408494-98-4P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tyrosyl-phospho peptides as inhibitors of secondary phosphorylation of HS1 protein)

IT **408494-97-3P 408501-56-4P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of tyrosyl-phospho peptides as inhibitors of secondary phosphorylation of HS1 protein)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:327572 HCAPLUS
DOCUMENT NUMBER: 135:29423
TITLE: Structural analysis of the role of the β3 subunit of the αVβ3 integrin in IGF-I signaling
AUTHOR(S): Maile, Laura A.; Badley-Clarke, Jane; Clemmons, David R.
CORPORATE SOURCE: Division of Endocrinology, University of North Carolina, Chapel Hill, NC, 27599-7170, USA
SOURCE: Journal of Cell Science (2001), 114(7), 1417-1425
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The disintegrin echistatin inhibits ligand occupancy of the αVβ3 integrin and reduces insulin-like growth factor I (IGF-I) stimulated migration, DNA synthesis, and receptor autophosphorylation in smooth muscle cells. This suggests that ligand occupancy of the αVβ3 receptor is required for full activation of the IGF-I receptor. Transfection of the full-length β3 subunit into CHO cells that have no endogenous β3 and do not migrate in response to IGF-I was sufficient for IGF-I to stimulate migration of these anchorage dependent cells. In contrast, transfection of either of two truncated mutant forms of β3 (terminating at W715 or E731) or a mutant with substitutions for Tyr747 Tyr759 (YY) into either CHO or into porcine smooth muscle cells did not restore the capacity of these cells to migrate across a surface in response to IGF-I. This effect was not due to loss of IGF-I receptor autophosphorylation since the response of the receptor to IGF-I was similar in cells expressing either the full-length or any of the mutant forms of the β3 subunit. Echistatin reduced IGF-I receptor phosphorylation in cells expressing the full-length or the YY mutant forms of β3 subunit, but it had no effect in cells expressing either of two truncated forms of β3. A **cell-permeable** peptide homologous to the C-terminal region of the β3 subunit (amino acids 747-762) reduced IGF-I stimulated migration and receptor autophosphorylation of non-transfected porcine smooth muscle cells. These results demonstrate that the full-length β3 with intact tyrosines at positions 747 and 759 is required

for CHO cells to migrate in response to IGF-I. Furthermore, a region of critical amino acids between residues 742-762 is required for echistatin to induce its regulatory effect on receptor phosphorylation. Since the IGF-I receptor does not bind to αVβ3 the results suggest that specific but distinct regions of the β3 subunit interact with intermediary proteins to facilitate IGF-I stimulated cell migration and echistatin induced inhibition of IGF-I signal transduction.

IT **182752-56-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(747-759-integrin β3; structural anal. of role of β3 subunit of αVβ3 integrin in IGF-I signaling)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:241473 HCAPLUS
DOCUMENT NUMBER: 135:87255
TITLE: Y-receptor affinity modulation by the design of pancreatic polypeptide/neuropeptide Y chimera led to Y5-receptor ligands with picomolar affinity
AUTHOR(S): Cabrele, C.; Wieland, H. A.; Langer, M.; Stidsen, C. E.; Beck-Sickinger, A. G.
CORPORATE SOURCE: Department of Applied Bioscience, Winterthurerstrasse 190, ETH Zurich, Zurich, 8057, Switz.
SOURCE: Peptides (New York, NY, United States) (2001), 22(3), 365-378
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuropeptide Y (NPY) and pancreatic polypeptide (PP) bind to the Y-receptors with very different affinities: NPY has high affinity for the receptors Y1, Y2 and Y5, while PP binds only to Y4-receptor with picomolar affinity. By exchanging of specific amino acid positions between the two peptides, we developed 38 full-length PP/NPY chimeras with binding properties that are completely different from those of the two native ligands. Pig NPY (pNPY) analogs containing the segment 19-23 from human PP (hPP) bound to the Y-receptors with much lower affinity than NPY itself. The affinity of the hPP analog containing the pNPY segments 1-7 and 19-23 was comparable to that of pNPY at the Y1- and Y5-receptor subtypes, and to that of hPP at the Y4-receptor. Furthermore, the presence of the segments 1-7 from chicken PP (**cPP**) and 19-23 from pNPY within the hPP sequence led to a ligand with IC50 of 40 pM at the Y5-receptor. This is the most potent Y5-receptor ligand known so far, with 15-fold higher affinity than NPY.

IT **264913-85-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(pancreatic polypeptide/neuropeptide Y chimera design of Y5 receptor ligands with picomolar affinity)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:553708 HCAPLUS
DOCUMENT NUMBER: 133:173015
TITLE: Production of protein particles that increase **cell permeability** for gene therapy
INVENTOR(S): Hildt, Eberhard; Hofschneider, Peter
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046376	A2	20000810	WO 2000-DE363	20000204
WO 2000046376	A3	20001116		
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19904800	C1	20010208	DE 1999-19904800	19990205
EP 1165797	A2	20020102	EP 2000-909000	20000204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: DE 1999-19904800 A 19990205
WO 2000-DE363 W 20000204

AB The invention relates to particles comprising: (a) a protein membrane with a fusion protein which comprises a virus protein, a **cell-permeability**-mediating peptide and a heterologous cell-specific binding site; and (b) a nucleic acid which is contained in the protein membrane and presents sequences for a virus-specific packaging signal and a structural gene. The invention also relates to methods for producing such particles, means suitable for this purpose and the use of the particles in gene therapy.

IT **267007-59-0**
RL: PRP (Properties)
(unclaimed sequence; production of protein particles that increase **cell permeability** for gene therapy)

L7 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:314843 HCAPLUS
DOCUMENT NUMBER: 132:331146
TITLE: A peptide mediating **cell permeability** from the hepatitis B virus pre-S antigen
INVENTOR(S): Hildt, Eberhard; Schmidt, Stephanie
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026379	A2	20000511	WO 1999-DE3506	19991103
WO 2000026379	A3	20001005		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19850718	C1	20000518	DE 1998-19850718	19981103
EP 1127133	A2	20010829	EP 1999-963187	19991103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528120	T2	20020903	JP 2000-579751	19991103

PRIORITY APPLN. INFO.: DE 1998-19850718 A 19981103
WO 1999-DE3506 W 19991103

OTHER SOURCE(S): MARPAT 132:331146

AB A **cell-permeable** polypeptide that can mediate **cell permeability** to substances, DNA coding for said polypeptide and a method for the production of said polypeptide are described. The invention also relates to antibodies directed against said polypeptide and the use of said polypeptide in the mediation of **cell permeability** to substances. The peptide is derived from the hepatitis B virus pre-S antigen.

IT **267007-59-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; peptide mediating **cell permeability** from hepatitis B virus pre-S antigen)

IT **267236-85-1**
RL: PRP (Properties)
(unclaimed sequence; peptide mediating **cell permeability** from the hepatitis B virus pre-S antigen)

L7 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:303286 HCAPLUS
DOCUMENT NUMBER: 133:72618
TITLE: Novel **cell permeable** motif derived from the PreS2-domain of hepatitis-B virus surface antigens
AUTHOR(S): Oess, S.; Hildt, E.
CORPORATE SOURCE: Max-Planck-Institut fur Biochemie, AG Virusforschung, Martinsried, Germany
SOURCE: Gene Therapy (2000), 7(9), 750-758
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Efficient transfer of proteins or nucleic acids across cellular membranes is a major problem in cell biol. Recently the existence

of a fusogenic sequence was predicted in the junction area of the PreS2- and S-domain of the hepatitis-B virus surface antigens. We have identified **cell permeability** as a novel property of the PreS2-domain. **Cell permeability** of PreS2 is not restricted to hepatocytes. PreS2 translocates in an energy-independent manner into cells and is evenly distributed over the cytosol. Detailed anal. revealed that **cell-permeability** is mediated by an amphipathic α-helix between amino acids 41 and 52 of PreS2. Destruction of this translocation motif (PreS2-TLM) abolishes **cell permeability**. PreS2-TLM per se can act as a shuttle for peptides and functional proteins (such as EGFP). This permits the highly specific modulation of intracellular signal transduction by transfer of peptides competing protein-protein interactions as demonstrated by specific inhibition of TNFα-dependent activation of c-Raf-1 kinase. Moreover, in vivo functionality was demonstrated by PreS2-TLM-dependent protein transfer into primary bone marrow cells and into the liver. The amphipatic motif is conserved between the different hepatitis-B virus subtypes, and the surface proteins of avian and rodent hepadnaviruses exhibit similar amphipatic peptide sequences. In respect to hepatitis-B virus-infection, the PreS2-TLM could represent the postulated fusion peptide and play a crucial role in the internalization of the viral particle.

IT **267007-59-0**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(novel **cell permeable** motif derived from the PreS2-domain of hepatitis-B virus surface antigens)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:122742 HCAPLUS
DOCUMENT NUMBER: 132:319992
TITLE: Biochemical, molecular and physiological characterization of a new β-casein variant detected in korean cattle
AUTHOR(S): Han, S. K.; Shin, Y. C.; Byun, H. D.
CORPORATE SOURCE: Department of Dairy Science, College of Animal Husbandry, KonKuk University, Seoul, S. Korea
SOURCE: Animal Genetics (2000), 31(1), 49-51
CODEN: ANGEE3; ISSN: 0268-9146
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There are seven known genetic variants of bovine β-casein (β-CN) - A1, A2, A3, B, C, D and E. In this study, we identified a new genetic variant (named β-CN H) which migrates slower than the other variants in acidic starch gel electrophoresis. We confirmed through protein and DNA sequence analyses that the H variant differs at five residues from the A2 sequence: Arg25/Cys, Leu88/Ile, Gln117/Glu, Glu175/Gln and Gln195/Glu. Of these substitutions the 25th residue was contained in the casein phospho-peptide (**CPP**) region. In rats, calcium solubilizing effect of the **CPP** of bovine variant H was

increased by ≈ 23% compared with that of the **CPP** of non-H. Using extensive Korean Bos taurus pedigrees, we confirmed that β-CN H was controlled by a codominant allele.

IT **267004-06-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; biochem., mol. and physiol. characterization of a new β-casein variant detected in Korean cattle)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:671973 HCAPLUS
DOCUMENT NUMBER: 132:11258
TITLE: A peptide representing the carboxyl-terminal tail of the Met receptor inhibits kinase activity and invasive growth
AUTHOR(S): Bardelli, Alberto; Longati, Paola; Williams, Tracy A.; Benvenuti, Silvia; Comoglio, Paolo M.
CORPORATE SOURCE: Institute for Cancer Research and Treatment (IRCC), School of Medicine, University of Torino, Candiolo, 10060, Italy
SOURCE: Journal of Biological Chemistry (1999), 274(41), 29274-29281
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interaction of the hepatocyte growth factor (HGF) with its receptor, the Met tyrosine kinase, results in invasive growth, a genetic program essential to embryonic development and implicated in tumor metastasis. Met-mediated invasive growth requires autophosphorylation of the receptor on tyrosines located in the kinase activation loop (Tyr1234-Tyr1235) and in the carboxyl-terminal tail (Tyr1349-Tyr1356). We report that peptides derived from the Met receptor tail, but not from the activation loop, bind the receptor and inhibit the kinase activity in vitro. Cell delivery of the tail receptor peptide impairs HGF-dependent Met phosphorylation and downstream signaling. In normal and transformed epithelial cells, the tail receptor peptide inhibits HGF-mediated invasive growth, as measured by cell migration, invasiveness, and branched morphogenesis. The Met tail peptide inhibits the closely related Ron receptor but does not significantly affect the epidermal growth factor, platelet-derived growth factor, or vascular endothelial growth factor receptor activities. These expts. show that carboxyl-terminal sequences impair the catalytic properties of the Met receptor, thus suggesting that in the resting state the nonphosphorylated tail acts as an intramol. modulator. Furthermore, they provide a strategy to selectively target the MET proto-oncogene by using small, **cell-permeable**, peptide derivs.

IT **251538-76-8P 251538-77-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(peptide representing C-terminal tail of Met receptor inhibits

kinase activity and invasive growth)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:390423 HCAPLUS
DOCUMENT NUMBER: 131:39724
TITLE: Cytotoxin fusion proteins for use in killing of cells infected by pathogens
INVENTOR(S): Dowdy, Steven F.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929721	A1	19990617	WO 1998-US26358	19981210
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2314267	AA	19990617	CA 1998-2314267	19981210
AU 9918182	A1	19990628	AU 1999-18182	19981210
EP 1037911	A1	20000927	EP 1998-963079	19981210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6221355	B1	20010424	US 1998-208966	19981210
JP 2002505077	T2	20020219	JP 2000-524312	19981210

PRIORITY APPLN. INFO.:
US 1997-69012P P 19971210
US 1998-82402P P 19980420
WO 1998-US26358 W 19981210

AB A method of controlling infection by killing infected cells is described.more fusion proteins that includes a transduction domain and a cytotoxic domain. The method uses fusion proteins of cytotoxins and a protein that directs entry into the cell (a transduction domain). The cytotoxic domain is specifically activated by a pathogen infection, e.g. by being processed by an infection-specific protease. Activation of the cytotoxin effectively kills or injures cells infected by one or a combination of different pathogens. The cytototoxin may be a protease or a prodrug-activating enzyme such as a thymidine kinase. In particular the method is directed at the treatment of HIV infection. Suitable transduction domains can be obtained from, inter alia, the tat protein, the Antennapedia gene product, and VP22 of herpes simplex virus. The method appears to be effective in transporting very large proteins into cells and can also tolerate a significant degree of unfolding or incorrect folding. A fusion protein of the TAT transduction domain and human caspase 3 (**CPP**-32) was shown to be effective at killing HIV-infected cells. The effect was

blocked by the HIV proteinase inhibitor Ritonavir, and mutation of the active site cysteine to methionine.

IT **227199-94-2D**, fusion products
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(as transduction doamin for import of cytotoxin zymogens; cytotoxin fusion proteins for use in killing of cells infected by pathogens)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:288457 HCAPLUS
DOCUMENT NUMBER: 131:82577
TITLE: Structural requirements for cellular uptake of α-helical amphipathic peptides
AUTHOR(S): Scheller, Anne; Oehlke, Johannes; Wiesner, Burkhard; Dathe, Margitta; Krause, Eberhard; Beyermann, Michael; Melzig, Mathias; Bienert, Michael
CORPORATE SOURCE: Institute of Molecular Pharmacology, Berlin, D 10315, Germany
SOURCE: Journal of Peptide Science (1999), 5(4), 185-194
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The structure of the **cell-permeable** α-helical amphipathic model peptide FLUOS-KLALKLALKALKAALKLA-NH2 (I) was modified stepwise with respect to its helix parameters hydrophobicity, hydrophobic moment and hydrophilic face as well as mol. size and charge. Cellular uptake and membrane destabilizing activity of the resulting peptides were studied using aortic endothelial cells and HPLC combined with CLSM. With the exceptions that a reduction of mol. size below 16 amino acid residues and the introduction of a neg. net charge abolished uptake, none of the investigated structural parameters proved to be essential for the passage of these peptides across the plasma membrane. Membrane toxicity also showed no correlation to any of the parameters investigated and could be detected only at concns. higher than 2 μM. These results implicate helical amphipathicity as the only essential structural requirement for the entry of such peptides into the cell interior, in accord with earlier studies. The pivotal role of helical amphipathicity was confirmed by uptake results obtained with two further pairs of amphipathic/non-amphipathic 18-mer peptides with different primary structure, net charge and helix parameters from I. The amphipathic counterparts were internalized into the cells to a comparable extent as I, whereas no cellular uptake could be detected for the non-amphipathic analogs. The mode of uptake remains unclear and involves both temperature-sensitive and -insensitive processes, indicating non-endocytic contributions.

IT **229482-14-8 229482-16-0**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structural requirements for cellular uptake and membrane

toxicity of α-helical amphipathic peptides)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:141765 HCAPLUS
DOCUMENT NUMBER: 131:126593
TITLE: Induction of seizures by the potent K+ channel-blocking scorpion venom peptide toxins tityustoxin-Kα and pandinustoxin-Kα
AUTHOR(S): Juhng, K. N.; Kokate, T. G.; Yamaguchi, S.; Kim, B. Y.; Rogowski, R. S.; Blaustein, M. P.; Rogawski, M. A.
CORPORATE SOURCE: National Institute of Neurological Disorders and Stroke, Epilepsy Research Branch, Neuronal Excitability Section, National Institutes of Health, Bethesda, MD, 20892-1408, USA
SOURCE: Epilepsy Research (1999), 34(2-3), 177-186
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The scorpion venom peptide toxins tityustoxin-Kα (TsTx-Kα) and pandinustoxin-Kα (PiTx-Kα) are novel, highly potent and selective blockers of voltage-activated K+ channels. PiTx-Kα preferentially blocks rapidly inactivating (A-type) K+ channels whereas TsTx-Kα is selective for slowly inactivating (delayed rectifier-type) channels. K+ channel blockers are known to induce seizures, but the specific K+ channel types that can serve as convulsant targets are not well defined. To address this issue, we examined for convulsant activity the K+ channel type-specific scorpion toxins and the selective K+ channel antagonists 4-aminopyridine (4-AP), an inhibitor of A-type voltage-activated K+ channels, and paxilline, a selective blocker of large conductance (maxi K) Ca2+-activated K+ channels. Intracerebroventricular injection of recombinant TsTx-Kα and PiTx-Kα in mice produced limbic and clonic-tonic seizures. The severity of the seizures increased during the 60-min period following injection, culminating in continuous clonic seizure activity (status epilepticus), tonic hind-limb extension, and eventually in death. The estimated doses producing limbic and clonic seizures in 50% of animals (CD50) for TsTx-Kα and PiTx-Kα were 9 and 33 ng, resp. 4-AP produced seizure activity similar to the toxins (CD50, 76 ng) whereas paxilline failed to induce seizures at doses up to 13.5 μg. Carbamazepine protected fully against the toxin- and 4-AP-induced seizures whereas phenytoin had variable activity against the clonic component although it was protective against tonic hind-limb extension. The AMPA receptor antagonist GYKI 52466 also conferred full protection against toxin-induced seizures, but the NMDA receptor antagonists (R)-**CPP** and dizocilpine failed to affect limbic and clonic seizures, although they protected against hind-limb extension. We conclude that selective blockade of delayed rectifier- or A-type voltage-activated K+ channels can produce limbic, clonic and tonic seizures, whereas blockade of maxi K-type Ca2+-activated K+ channels does not. The convulsant effects may be related to enhanced glutamate release and, in the case of the limbic and clonic

convulsions, activation of AMPA receptors.

IT **185529-64-0**, Pandinustoxin Kα
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(185529640; induction of seizures by potent K+ channel-blocking scorpion venom peptide toxins tityustoxin-Kα and pandinustoxin-Kα)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:42577 HCAPLUS
DOCUMENT NUMBER: 130:105333
TITLE: Calcium blockers to treat proliferative vitreoretinopathy
INVENTOR(S): Dreyer, Evan B.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900129	A1	19990107	WO 1998-US12414	19980615
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9879672	A1	19990119	AU 1998-79672	19980615
AU 727080	B2	20001130		
EP 994709	A1	20000426	EP 1998-930231	19980615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511868	T2	20020416	JP 1999-505580	19980615
US 6380261	B1	20020430	US 1999-445832	19991213
US 2003060510	A1	20030327	US 2002-38215	20020102
US 6573280	B2	20030603		
US 2003199551	A1	20031023	US 2003-436902	20030512

PRIORITY APPLN. INFO.:
US 1997-51962P P 19970630
WO 1998-US12414 W 19980615
US 1999-445832 A1 19991213
US 2002-38215 A1 20020102

AB Glutamate causes migration and proliferation of retinal pigment epithelium and/or glial cells, and glutamate antagonists can prevent, treat or reduce retinal pigment epithelium and/or glial migration and the subsequent development of proliferative vitreoretinopathy. Avoidance or management of proliferative vitreoretinopathy can be achieved by administration to the patient of a compound capable of reducing glutamate-induced retinal cell

migration in a concentration effective to reduce such migration.

IT **107452-89-1**, SNX-111
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as agents decreasing glutamate release; calcium blockers to treat proliferative vitreoretinopathy)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:534565 HCAPLUS
DOCUMENT NUMBER: 129:260833
TITLE: Preparation of functionally active **cell-permeable** peptides by single-step ligation of two peptide modules
AUTHOR(S): Zhang, Lianshan; Torgerson, Troy R.; Liu, Xue-Yan; Timmons, Sheila; Colosia, Ann D.; Hawiger, Jacek; Tam, James P.
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University, Nashville, TN, 37232-2363, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(16), 9184-9189
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Noninvasive cellular import of synthetic peptides can be accomplished by incorporating a hydrophobic, membrane-permeable sequence (MPS). Herein, the authors describe a facile method that expedites synthesis of biol. active, **cell-permeable** peptides by site-specific ligation of two free peptide modules: one bearing a functional sequence and the second bearing a MPS. A nonpeptide thiazolidino linkage between the two modules is produced by ligation of the C-terminal aldehyde on the MPS and the N-terminal 1,2-aminothiol moiety on the functional sequence. This thiazolidine ligation approach is performed with stoichiometric amts. of fully unprotected MPS and functional peptide in an aqueous buffered solution, eliminating the need for addnl. chemical manipulation and purification prior to use in bioassays. Two different MPSs were interchangeably combined with two different functional sequences to generate two sets of hybrid peptides. One set of hybrid peptides, carrying the cytoplasmic cell adhesion regulatory domain of the human integrin β3, inhibited adhesion of human erythroleukemia cells to fibrinogen-coated surfaces. A second set of hybrid peptides, carrying the nuclear localization sequence of the transcription factor NF-κB, inhibited nuclear import of transcription factors NF-κB, activator protein 1, and nuclear factor of activated T cells in agonist-stimulated Jurkat T lymphocytes. In each assay, these nonamide bond hybrids were found to be functionally comparable to peptides prepared by the conventional method. Cumulatively, this new ligation approach provides an easy and rapid method for engineering of functional, **cell-permeable** peptides and demonstrates the potential for synthesis of **cell-permeable** peptide libraries designed to block intracellular protein-protein interactions.

IT **213546-56-6**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of functionally active **cell-permeable** peptides by single-step ligation of two peptide modules)

IT **213546-42-0P 213546-45-3P 213546-48-6P 213546-50-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of functionally active **cell-permeable** peptides by single-step ligation of two peptide modules)

IT **213546-28-2P 213546-31-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of functionally active **cell-permeable** peptides by single-step ligation of two peptide modules)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:251067 HCAPLUS
DOCUMENT NUMBER: 128:304071
TITLE: Method for disrupting cellular adhesion using peptides with a cell adhesion regulatory domain of an adhesion receptor or counter receptor
INVENTOR(S): Hawiger, Jack J.; Timmons, Sheila; Liu, Xue-Yan
PATENT ASSIGNEE(S): Vanderbilt University, USA; Hawiger, Jack J.; Timmons, Sheila; Liu, Xue-Yan
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816241	A1	19980423	WO 1997-US18331	19971009
W: AU, CA, US				
AU 9748153	A1	19980511	AU 1997-48153	19971009

PRIORITY APPLN. INFO.: US 1996-28420P P 19961015
WO 1997-US18331 W 19971009

AB A method is provided for inhibiting or disrupting cellular adhesion of a cell, comprising transferring into the cell a polypeptide comprising a cell adhesion regulatory domain of an adhesion receptor or counter receptor expressed by the cell. In particular, a method is provided for inhibiting or disrupting cellular adhesion of a cell comprising transferring into the cell a polypeptide comprising a cell adhesion regulatory domain of a subunit, i.e., the α-subunit or the β-subunit of an integrin expressed by the cell.

IT **153421-75-1 182752-56-3 206748-53-0 206748-54-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides with cell adhesion regulatory domain of adhesion

receptor or counter receptor for cell adhesion disruption)

IT **206770-27-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(peptides with cell adhesion regulatory domain of adhesion receptor or counter receptor for cell adhesion disruption)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:106030 HCAPLUS
DOCUMENT NUMBER: 128:162866
TITLE: Peptides derived from double-stranded RNA-dependent protein kinase for promotion of proliferation of cells and tissues in a controlled manner
INVENTOR(S): Bottaro, Donald P.; Petryshyn, Raymond
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Bottaro, Donald P.; Petryshyn, Raymond
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804717	A2	19980205	WO 1997-US14350	19970729
WO 9804717	A3	19980305		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9739824	A1	19980220	AU 1997-39824	19970729
US 6326466	B1	20011204	US 1999-230548	19990723

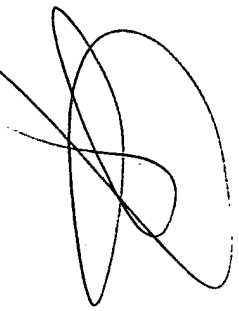
PRIORITY APPLN. INFO.: US 1996-23307P P 19960730
WO 1997-US14350 W 19970729

AB Peptides derived from double-stranded RNA dependent protein kinase (PKR) that act as antagonists are described. More specifically, they antagonize activation of double-stranded RNA dependent protein kinase (PKR) by binding to the activator RNA and stimulate eukaryotic cell proliferation under conditions of cell cycle arrest, quiescence, reduced growth or cell death. These antagonists can be used to protect cells from HIV-1 pathogenesis by preventing TAR RNA binding to the enzyme.

IT **203065-48-9D**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antagonist of double-stranded RNA-dependent protein kinase; peptides derived from double-stranded RNA-dependent protein

kinase for promotion of proliferation of cells and tissues in controlled manner)

L7 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:577756 HCAPLUS
DOCUMENT NUMBER: 127:257993
TITLE: Selective inhibition of growth factor-stimulated mitogenesis by a **cell-permeable** Grb2-binding peptide
AUTHOR(S): Williams, Emma J.; Dunican, Dara J.; Green, Paul J.; Howell, Fiona V.; Derossi, Daniele; Walsh, Frank S.; Doherty, Patrick
CORPORATE SOURCE: Dep. Experimental Pathology, United Med. and Dental Sch., Guy's Hosp., London, SE1 9RT, UK
SOURCE: Journal of Biological Chemistry (1997), 272(35), 22349-22354
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English



AB The activation of the mitogen-activated protein kinase (MAPK) cascade by a variety of growth factors and other agents is central to a mitogenic response. In the case of polypeptide growth factors such as the epidermal growth factor (EGF) and platelet-derived growth factor (PDGF), the steps leading to activation of MAPK require the function of the adaptor protein Grb2 (growth factor receptor binding protein 2), which can bind either directly or indirectly via its Src homol. 2 domain to activated receptor tyrosine kinases. A **cell-permeable** mimetic of the EGF receptor Grb2 binding site has been investigated for its ability to inhibit biol. responses stimulated by a variety of growth factors. Pretreatment of cells with this peptide results in the accumulation of the peptide in cells and its association with Grb2. This is associated with a complete inhibition of the mitogenic response stimulated by EGF and PDGF. In contrast, the peptide has no effect on the mitogenic response stimulated by fibroblast growth factor. The peptide could also inhibit the phosphorylation of MAPK stimulated with EGF and PDGF in the absence of an effect on the fibroblast growth factor response. These data demonstrate that **cell-permeable** mimetics of Src homol. 2 binding sites can selectively inhibit growth factor-stimulated mitogenesis, and also directly demonstrate specificity in the coupling of activated receptor tyrosine kinases to the MAPK cascade.

IT **196216-55-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(selective inhibition of growth factor-stimulated mitogenesis by a **cell-permeable** Grb2-binding peptide)

L7 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:142639 HCAPLUS
DOCUMENT NUMBER: 126:233779
TITLE: Protein kinase A-anchoring inhibitor peptides arrest mammalian sperm motility
AUTHOR(S): Vijayaraghavan, Srinivasan; Goueli, Said A.; Davey, Michael P.; Carr, Daniel W.
CORPORATE SOURCE: Oregon Regional Primate Research Center,

Beaverton, OR, 97006, USA
SOURCE: Journal of Biological Chemistry (1997), 272(8), 4747-4752
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protein kinase A (PKA) is anchored at specific subcellular sites through the interaction of the regulatory subunit (R) with protein kinase A-anchoring proteins (AKAPs) via an amphipathic helix binding motif. Synthetic peptides containing this amphipathic helix domain competitively disrupt PKA binding to AKAPs and cause a loss of PKA modulation of cellular responses. In this report we use S-Ht31, a cell-permeant anchoring inhibitor peptide, to study the role of PKA anchoring in sperm. Our anal. of three species of mammalian sperm detected three isoforms of PKA (RIIα, RIIβ, and RIβ) and one 110-kDa AKAP. The addition of S-Ht31 to bovine caudal epididymal sperm inhibits motility in a time- and concentration-dependent manner. A control peptide, S-Ht31-P, identical to S-Ht31 except for a proline for isoleucine substitution to prevent amphipathic helix formation, had no effect on motility. The inhibition of motility by S-Ht31 is reversible but only if calcium is present in the suspension buffer, suggesting a role for PKA anchoring in regulating cellular calcium homeostasis. Surprisingly, inhibition of PKA catalytic activity had little effect on basal motility or motility stimulated by agents previously thought to work via PKA activation. These data suggest that the interaction of the regulatory subunit of PKA with sperm AKAPs, independent of PKA catalytic activity, is a key regulator of sperm motility and that disruption of this interaction using **cell-permeable** anchoring inhibitor peptides may form the basis of a sperm-targeted contraceptive.

IT **188425-80-1 188425-81-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(protein kinase A-anchoring inhibitor peptides arrest mammalian sperm motility)

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:632519 HCAPLUS
DOCUMENT NUMBER: 125:268630
TITLE: Identification of a functionally important sequence in the cytoplasmic tail of integrin β3 by using **cell-permeable** peptide analogs
AUTHOR(S): Liu, Xue-Yan; Timmons, Sheila; Lin, Yao-Zhong; Hawiger, Jacek
CORPORATE SOURCE: Dep. Microbiol. Immunol., Vanderbilt Univ. Sch. Med., Nashville, TN, 37232, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(21), 11819-11824
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Integrins are major two-way signaling receptors responsible for the attachment of cells to the extracellular matrix and for cell-cell interactions that underlie immune responses, tumor metastasis, and progression of atherosclerosis and thrombosis. We report the structure-function anal. of the cytoplasmic tail of integrin β3 (glycoprotein IIIa) based on the cellular import of synthetic peptide analogs of this region. Among the four overlapping **cell-permeable** peptides, only the peptide carrying residues 747-762 of the carboxyl-terminal segment of integrin β2 inhibited adhesion of human erythroleukemia (HEL) cells and of human endothelial cells (ECV) 304 to immobilized fibrinogen mediated by integrin β3 heterodimers, αIIbβ3, and αvβ3, resp. Inhibition of adhesion was integrin-specific because the **cell-permeable** β3 peptide (residues 747-762) did not inhibit adhesion of human fibroblasts mediated by integrin β1 heterodimers. Conversely, a **cell-permeable** peptide representing homologous portion of the integrin β1 cytoplasmic tail (residues 788-803) inhibited adhesion of human fibroblasts, whereas it was without effect on adhesion of HEL or ECV 304 cells. The **cell-permeable** integrin β3 peptide (residues 747-762) carrying a known loss-of-function mutation (Ser752Pro) responsible for the genetic disorder Glanzmann thrombasthenia Paris I did not inhibit cell adhesion of HEL or ECV 304 cells, whereas the β3 peptide carrying a Ser752Ala mutation was inhibitory. Although Ser752 is not essential, Tyr747 and Tyr759 form a functionally active tandem because conservative mutations Tyr747Phe or Tyr759Phe resulted in a nonfunctional **cell permeable** integrin β3 peptide. We propose that the carboxyl-terminal segment of the integrin β3 cytoplasmic tail spanning residues 747-762 constitutes a major intracellular cell adhesion regulatory domain (CARD) that modulates the interaction of integrin β3-expressing cells with immobilized fibrinogen. Import of **cell-permeable** peptides carrying this domain results in inhibition "from within" of the adhesive function of these integrins.

IT **182752-56-3**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(functionally important sequence in the cytoplasmic tail of integrin β3)

L7 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:204737 HCAPLUS
DOCUMENT NUMBER: 124:314980
TITLE: Intramolecular inhibition of human defensin HNP-1 by its propiece
AUTHOR(S): Valore, Erika V.; Martin, Edith; Harwig, Sylvia S. L.; Ganz, Tomas
CORPORATE SOURCE: Will Rogers Institute Pulmonary Res. Laboratory, UCLA School Medicine, Los Angeles, CA, 90095-1736, USA
SOURCE: Journal of Clinical Investigation (1996), 97(7), 1624-9
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examined mechanisms that protect host defense cells from their cytotoxic effector mols. Human neutrophil peptides (HNP) 1-3 are microbicidal and cytotoxic defensins, initially synthesized as 94-amino acid preproHNP1-94, cotranslationally proteolyzed to proHNP20-94, then converted by removal of the anionic propiece to mature HNP65-94 (HNP-1 and -3) and HNP66-94 (HNP-2). The authors hypothesized that during synthesis and subcellular sorting the anionic propiece inhibits the cytotoxicity of the cationic defensin. The authors expressed preproHNP-1 cDNA in recombinant baculovirus-infected insect cells that secreted the normally transient proHNP-120-94 into the medium. Cyanogen bromide cleaved proHNP-120-94 at the fortuitously located Met64 to yield mature recombinant HNP-165-94 and unlinked propiece. Recombinant and native HNP-1 purified from PMN were identical as judged by mass spectrometry, retention time in reverse-phase high performance liquid chromatog., migration on acid-urea polyacrylamide gels, and reaction with a conformation-specific antibody. Recombinant and native HNP-1 had comparable microbicidal activity towards Listeria monocytogenes and were similarly potent in permeabilizing K562 leukemia cells, but proHNP-120-94 was virtually inactive in both assays. Addition of unlinked propiece (proHNP-120-64 with Met64→homoserine) inhibited the bactericidal and **cell-permeabilizing** activity of mature HNP-1 in a dose-dependent manner. Linked, and to a lesser extent unlinked, propiece interfered with the binding of HNP-1 to target cells. The propiece thus acts as an efficient intramol. inhibitor of defensin HNP-1 cytotoxicity.

IT **162261-10-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(intramol. inhibition of human neutrophil defensin HNP-1 cytotoxicity by its propiece)

E1 THROUGH E61 ASSIGNED

FILE 'REGISTRY' ENTERED AT 11:30:32 ON 07 NOV 2003
L8 61 SEA FILE=REGISTRY ABB=ON PLU=ON (182752-56-3/BI OR 267007-59-0/BI OR 227199-94-2/BI OR 107452-89-1/BI OR 118997-30-1/BI OR 153421-75-1/BI OR 162261-10-1/BI OR 175735-93-0/BI OR 185529-64-0/BI OR 186420-62-2/BI OR 188425-80-1/BI OR 188425-81-2/BI OR 189036-95-1/BI OR 196216-55-4/BI OR 203065-48-9/BI OR 206748-53-0/BI OR 206748-54-1/BI OR 206770-27-6/BI OR 213546-28-2/BI OR 213546-31-7/BI OR 213546-42-0/BI OR 213546-45-3/BI OR 213546-48-6/BI OR 213546-50-0/BI OR 213546-56-6/BI OR 229482-14-8/BI OR 229482-16-0/BI OR 251538-76-8/BI OR 251538-77-9/BI OR 264913-85-1/BI OR 267004-06-8/BI OR 267236-85-1/BI OR 408494-97-3/BI OR 408494-98-4/BI OR 408501-56-4/BI OR 427884-67-1/BI OR 427884-68-2/BI OR 478550-79-7/BI OR 478550-80-0/BI OR 482371-23-3/BI OR 482371-24-4/BI OR 482371-25-5/BI OR 489473-07-6/BI OR 491599-42-9/BI OR 491599-43-0/BI OR 491599-44-1/BI OR 491599-47-4/BI OR 491599-64-5/BI OR 491599-65-6/BI OR 491599-66-7/BI OR 528846-93-7/BI OR 528847-09-8/BI OR 528847-14-5/BI OR 528847-21-4/BI OR 528900-10-9/BI OR 528900-12-1/BI OR 528900-13-2/BI OR 528900-21-2/BI OR

528900-28-9/BI OR 528900-30-3/BI OR 528900-31-4/BI)

L9 61 L8 AND L1

L9 ANSWER 1 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528900-31-4** REGISTRY
CN L-Valine, L-seryl-L-histidyl-L-lysyl-L-glutaminyl-L-glutaminyl-L-prolyl-L-seryl-L-seryl-L-threonyl-L-prolyl-L-α-glutamyl-L-lysyl-L-arginyl-L-arginyl-L-threonyl-L-seryl-L-leucyl-L-isoleucyl-L-prolyl-L-arginyl-L-prolyl-L-lysyl-L-seryl-L-prolyl-L-asparaginyl-L-methionyl-L-glutaminyl-L-α-aspartyl-L-leucyl-L-lysyl-L-arginyl-L-arginyl-L-phenylalanyl-L-lysyl-L-glutaminyl-L-alanyl-L-leucyl-L-seryl-L-alanyl-L-lysyl-L-valyl-L-arginyl-L-threonyl-L-valyl-L-threonyl-L-seryl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 97: PN: WO03042239 TABLE: 1 claimed protein
CI MAN
SQL 47

SEQ 1 SHKQQPSSTP EKRRTSLIPR PKSPNMQDLK RRFKQALSAK VRTVTSV
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HITS AT: 26-35

REFERENCE 1: 139:2887

L9 ANSWER 2 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528900-30-3** REGISTRY
CN L-Serine, L-arginyl-L-arginyl-L-arginyl-L-methionyl-L-valyl-L-glutaminylglycyl-L-lysyl-L-threonyl-L-arginyl-L-arginyl-L-arginyl-L-seryl-L-seryl-L-threonyl-L-threonyl-L-histidyl-L-valyl-L-lysyl-L-glutaminyl-L-alanyl-L-isoleucyl-L-asparaginyl-L-lysyl-L-methionyl-L-leucyl-L-threonyl-L-lysyl-L-isoleucyl-L-seryl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 96: PN: WO03042239 TABLE: 1 claimed protein
CI MAN
SQL 31

SEQ 1 RRRMVQGKTR RRSSTTHVKQ AINKMLTKIS S
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HITS AT: 18-31

REFERENCE 1: 139:2887

L9 ANSWER 3 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528900-28-9** REGISTRY
CN L-Tyrosine, L-tyrosyl-L-seryl-L-α-aspartyl-L-threonyl-L-glutaminyl-L-glutaminyl-L-glutaminyl-L-prolyl-L-lysyl-L-lysyl-L-seryl-L-lysyl-L-seryl-L-arginyl-L-threonyl-L-prolyl-L-α-aspartyl-L-lysyl-L-methionyl-L-lysyl-L-asparaginyl-L-leucyl-L-seryl-L-lysyl-L-seryl-L-tryptophyl-L-tryptophyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 91: PN: WO03042239 TABLE: 1 claimed protein
CI MAN
SQL 30

SEQ 1 YSDTQQQPKK SKSRTPDKMK NLSKSWWKKY

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HITS AT:    19-28

REFERENCE   1:  139:2887

L9   ANSWER 4 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   528900-21-2  REGISTRY
CN   L-Serine, L-seryl-L-tyrosyl-L-lysyl-L-glutaminyl-L-asparaginyl-L-
     seryl-L-glutaminyl-L-α-aspartyl-L-phenylalanyl-L-methionyl-L-
     α-aspartyl-L-α-glutamyl-L-isoleucyl-L-phenylalanyl-L-
     glutaminyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-L-
     asparaginyl-L-phenylalanyl-L-seryl-L-leucyl-L-α-glutamyl-L-
     glutaminyl-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-
     L-α-aspartyl-L-valyl-L-prolyl-L-α-aspartyl-L-glutaminyl-
     L-α-glutamyl-L-glutaminyl-L-seryl-L-seryl-L-seryl-L-isoleucyl-
     L-α-glutamyl-L-threonyl-L-prolyl-L-seryl-L-α-glutamyl-L-
     α-glutamyl-L-alanyl-L-alanyl-L-seryl-L-prolyl-L-histidyl-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   60: PN: WO03042239 TABLE: 1 claimed protein
CI   MAN
SQL  50

SEQ      1 SYKQNSQDFM DEIFQELENF SLEQEEEDVP DQEQSSSIET PSEEAASPHS
                   = =========                      === ========
HITS AT:    10-19, 38-47

REFERENCE   1:  139:2887

L9   ANSWER 5 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   528900-13-2  REGISTRY
CN   Glycine, L-lysyl-L-isoleucyl-L-glutaminyl-L-α-glutamylglycyl-L-
     valyl-L-phenylalanyl-L-α-aspartyl-L-isoleucyl-L-asparaginyl-L-
     asparaginyl-L-α-glutamyl-L-alanyl-L-asparaginylglycyl-L-
     isoleucyl-L-lysyl-L-isoleucylglycyl-L-prolyl-L-glutaminyl-L-histidyl-
     L-alanyl-L-alanyl-L-threonyl-L-asparaginyl-L-alanyl-L-threonyl-L-
     histidyl-L-alanylglycyl-L-asparaginyl-L-glutaminylglycylglycyl-L-
     glutaminyl-L-glutaminyl-L-alanylglycylglycyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   34: PN: WO03042239 TABLE: 1 claimed protein
CI   MAN
SQL  41

SEQ      1 KIQEGVFDIN NEANGIKIGP QHAATNATHA GNQGGQQAGG G
                    = =========
HITS AT:    20-29

REFERENCE   1:  139:2887

L9   ANSWER 6 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   528900-12-1  REGISTRY
CN   L-Threonine, L-lysyl-L-lysyl-L-α-glutamyl-L-seryl-L-methionyl-
     L-prolyl-L-seryl-L-leucyl-L-methionyl-L-α-glutamyl-L-lysyl-L-
     lysyl-L-leucyl-L-lysyl-L-arginyl-L-lysyl-L-α-aspartyl-L-seryl-
     L-leucyl-L-tryptophyl-L-lysyl-L-lysyl-L-leucyl-L-lysylglycyl-L-seryl-
     L-leucyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-α-glutamyl-L-
     asparaginyl-L-methionyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
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CN 24: PN: WO03042239 TABLE: 1 claimed protein
CI MAN
SQL 35

SEQ 1 KKESMPSLME KKLKRKDSLW KKLKGSLKKK RENMT
= =========

HITS AT: 20-29

REFERENCE 1: 139:2887

L9 ANSWER 7 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528900-10-9** REGISTRY
CN L-Tyrosine, L-alanylglycyl-L-isoleucyl-L-glutaminyl-L-tyrosyl-L-seryl-L-α-aspartyl-L-threonyl-L-glutaminyl-L-glutaminyl-L-glutaminyl-L-prolyl-L-lysyl-L-lysyl-L-seryl-L-lysyl-L-seryl-L-arginyl-L-threonyl-L-prolyl-L-α-aspartyl-L-lysyl-L-methionyl-L-lysyl-L-asparaginyl-L-leucyl-L-seryl-L-lysyl-L-seryl-L-tryptophyl-L-tryptophyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: WO03042239 TABLE: 1 claimed protein
CI MAN
SQL 34

SEQ 1 AGIQYSDTQQ QPKKSKSRTP DKMKNLSKSW WKKY
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HITS AT: 23-32

REFERENCE 1: 139:2887

L9 ANSWER 8 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528847-21-4** REGISTRY
CN Glycine, L-alanyl-L-asparaginyl-L-α-glutamyl-L-cysteinyl-L-α-aspartyl-L-leucyl-L-methionyl-L-α-glutamyl-L-seryl-L-isoleucyl-L-α-glutamyl-L-prolyl-L-α-aspartyl-L-valyl-L-valyl-L-lysyl-L-prolyl-L-histidyl-L-leucyl-L-threonyl-L-seryl-L-threonyl-L-lysyl-L-valyl-L-alanyl-L-seryl-L-cysteinyl-L-seryl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 74: PN: WO03042239 TABLE: 1 claimed protein
SQL 29

SEQ 1 ANECDLMESI EPDVVKPHLT STKVASCSG
==== ======

HITS AT: 7-16

REFERENCE 1: 139:2887

L9 ANSWER 9 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528847-14-5** REGISTRY
CN L-Arginine, L-prolyl-L-leucyl-L-α-aspartyl-L-prolyl-L-histidyl-L-α-glutamyl-L-asparaginylglycyl-L-asparaginyl-L-asparaginylglycyl-L-threonyl-L-isoleucyl-L-lysyl-L-valyl-L-α-glutamyl-L-lysyl-L-prolyl-L-threonyl-L-methionyl-L-glutaminyl-L-alanyl-L-seryl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 68: PN: WO03042239 TABLE: 1 claimed protein
SQL 25

SEQ 1 PLDPHENGNN GTIKVEKPTM QASRR
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HITS AT: 15-24

REFERENCE 1: 139:2887

L9 ANSWER 10 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528847-09-8** REGISTRY
CN L-Serine, L-glutaminyl-L-arginyl-L-seryl-L-methionyl-L-lysyl-L-alanyl-L-prolyl-L-seryl-L-α-glutamyl-L-prolyl-L-arginyl-L-phenylalanyl-L-arginyl-L-leucyl-L-histidyl-L-α-aspartyl-L-tyrosyl-L-valyl-L-lysyl-L-arginyl-L-α-glutamylglycyl-L-arginylglycyl-L-alanyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 63: PN: WO03042239 TABLE: 1 claimed protein
SQL 26

SEQ 1 QRSMKAPSEP RFRLHDYVKR EGRGAS
==== ======
HITS AT: 7-16

REFERENCE 1: 139:2887

L9 ANSWER 11 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **528846-93-7** REGISTRY
CN Glycine, L-glutaminyl-L-α-aspartyl-L-arginyl-L-seryl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-methionyl-L-isoleucyl-L-α-aspartyl-L-isoleucyl-L-lysyl-L-leucyl-L-α-glutamyl-L-lysyl-L-prolyl-L-glutaminyl-L-α-glutamyl-L-glutaminyl-L-prolyl-L-valyl-L-seryl-L-α-glutamylglycyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 43: PN: WO03042239 TABLE: 1 claimed protein
SQL 25

SEQ 1 QDRSREDMID IKLEKPQEQP VSEGG
======== ==
HITS AT: 13-22

REFERENCE 1: 139:2887

L9 ANSWER 12 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-66-7** REGISTRY
CN L-Tryptophan, N2-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)carbonyl]-L-arginyl-L-arginyl-L-isoleucyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-prolyl-L-arginyl-L-leucyl-L-prolyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-prolyl-L-leucyl-(4S)-2-(hydroxymethyl)-4-oxazolidinecarbonyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (33→1')-thioether with N-(mercaptoacetyl)glycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 55,46,9

SEQ 1 RRIRPRPPRL PRPRPPLXVG PQPNEDTVTQ AACKVLTTGL PALISW

=== =======

HITS AT: 28-37

SEQ 1 GRAFVTIGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:137578

L9 ANSWER 13 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-65-6** REGISTRY
CN L-Tryptophan, L-arginyl-L-arginyl-L-isoleucyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-prolyl-L-arginyl-L-leucyl-L-prolyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-leucyl-(4S)-2-(hydroxymethyl)-4-oxazolidinecarbonyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (32→1')-thioether with N-(mercaptoacetyl)glycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 54,45,9

SEQ 1 RRIRPRPPRL PRPRPLXVGP QPNEDTVTQA ACKVLTTGLP ALISW
==== ======

HITS AT: 27-36

SEQ 1 GRAFVTIGK

REFERENCE 1: 139:7162

REFERENCE 2: 138:137578

L9 ANSWER 14 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-64-5** REGISTRY
CN L-Tryptophan, L-arginyl-L-arginyl-L-isoleucyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-prolyl-L-arginyl-L-leucyl-L-prolyl-L-arginyl-L-prolyl-L-arginyl-L-prolyl-L-prolyl-L-leucyl-(4S)-2-(hydroxymethyl)-4-oxazolidinecarbonyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (33→1')-thioether with N-(mercaptoacetyl)glycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 55,46,9

SEQ 1 RRIRPRPPRL PRPRPPLXVG PQPNEDTVTQ AACKVLTTGL PALISW
=== =======

HITS AT: 28-37

SEQ 1 GRAFVTIGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:137578

L9 ANSWER 15 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-47-4** REGISTRY
CN L-Tryptophan, L-prolyl-L-prolyl-L-prolyl-L-prolyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-α-aspartyl-L-prolyl-L-prolyl-L-prolyl-L-prolyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-α-aspartyl-L-leucylglycyl-(4S,5R)-2-(hydroxymethyl)-5-methyl-4-oxazolidinecarbonyl-L-isoleucyl-L-glutaminyl-L-lysyl-L-leucyl-L-α-glutamyl-L-α-aspartyl-L-methionyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (41→1')-thioether with N2-(mercaptoacetyl)-L-arginyl-L-isoleucyl-L-glutaminyl-L-arginylglycyl-L-prolylglycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 69,54,15

SEQ 1 PPPPNPNDPP PPNPNDLGXI QKLEDMVGPQ PNEDTVTQAA CKVLTTGLPA
=====
51 LISW
HITS AT: 36-45

SEQ 1 RIQRGPGRAF VTIGK

REFERENCE 1: 138:137578

L9 ANSWER 16 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-44-1** REGISTRY
CN L-Tryptophan, L-seryl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (16→1')-thioether with N-(mercaptoacetyl)glycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 38,29,9

SEQ 1 SVGPQPNEDT VTQAACKVLT TGLPALISW
==========
HITS AT: 11-20

SEQ 1 GRAFVTIGK

REFERENCE 1: 138:137578

L9 ANSWER 17 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-43-0** REGISTRY
CN L-Tryptophan, L-threonyl-L-isoleucyl-L-glutaminyl-L-lysyl-L-leucyl-L-α-glutamyl-L-α-aspartyl-L-methionyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl-, (23→1')-thioether with N2-(mercaptoacetyl)-L-arginyl-

L-isoleucyl-L-glutaminyl-L-arginylglycyl-L-prolylglycyl-L-arginyl-L-alanyl-L-phenylalanyl-L-valyl-L-threonyl-L-isoleucylglycyl-L-lysine (9CI) (CA INDEX NAME)
CI MAN
SQL 51,36,15

SEQ 1 TIQKLEDMVG PQPNEDTVTQ AACKVLTTGL PALISW
=== =======

HITS AT: 18-27

SEQ 1 RIQRGPGRAF VTIGK

REFERENCE 1: 138:137578

L9 ANSWER 18 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **491599-42-9** REGISTRY
CN L-Tryptophan, L-threonyl-L-isoleucyl-L-glutaminyl-L-lysyl-L-leucyl-L-α-glutamyl-L-α-aspartyl-L-methionyl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl- (9CI) (CA INDEX NAME)
CI MAN
SQL 36

SEQ 1 TIQKLEDMVG PQPNEDTVTQ AACKVLTTGL PALISW
=== =======

HITS AT: 18-27

REFERENCE 1: 138:137578

L9 ANSWER 19 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **489473-07-6** REGISTRY
CN L-Tryptophan, L-seryl-L-valylglycyl-L-prolyl-L-glutaminyl-L-prolyl-L-asparaginyl-L-α-glutamyl-L-α-aspartyl-L-threonyl-L-valyl-L-threonyl-L-glutaminyl-L-alanyl-L-alanyl-L-cysteinyl-L-lysyl-L-valyl-L-leucyl-L-threonyl-L-threonylglycyl-L-leucyl-L-prolyl-L-alanyl-L-leucyl-L-isoleucyl-L-seryl- (9CI) (CA INDEX NAME)
SQL 29

SEQ 1 SVGPQPNEDT VTQAACKVLT TGLPALISW
==========

HITS AT: 11-20

REFERENCE 1: 139:7162

REFERENCE 2: 138:137578

L9 ANSWER 20 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **482371-25-5** REGISTRY
CN L-Valine, L-alanyl-L-lysyl-L-tryptophyl-L-lysyl-L-threonyl-L-leucyl-L-leucyl-L-lysyl-L-lysyl-L-valyl-L-leucyl-L-lysyl-L-alanyl-L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-leucyl-L-lysyl- (9CI) (CA INDEX NAME)
SQL 21

SEQ 1 AKWKTLLKKV LKAPKKKRLK V

```
             ======== ==
HITS AT:    3-12

REFERENCE   1:  138:70348

L9   ANSWER 21 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   482371-24-4  REGISTRY
CN   L-Alanine, L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-arginyl-L-leucyl-L-
     lysyl-L-valyl-L-alanyl-L-lysyl-L-tryptophyl-L-lysyl-L-threonyl-L-
     leucyl-L-leucyl-L-lysyl-L-lysyl-L-valyl-L-leucyl-L-lysyl- (9CI)  (CA
     INDEX NAME)
SQL  21

SEQ      1 PKKKRLKVAK WKTLLKKVLK A
                       ==========
HITS AT:    11-20

REFERENCE   1:  138:70348

L9   ANSWER 22 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   482371-23-3  REGISTRY
CN   L-Cysteine, L-arginyl-L-α-aspartyl-L-lysyl-L-arginyl-L-
     glutaminyl-L-alanyl-L-arginyl-L-arginylglycyl-L-arginyl-L-arginyl-L-
     arginyl-L-alanyl-L-lysyl-L-tryptophyl-L-lysyl-L-threonyl-L-leucyl-L-
     leucyl-L-lysyl-L-lysyl-L-valyl-L-leucyl-L-lysyl-L-alanyl- (9CI)  (CA
     INDEX NAME)
SQL  26

SEQ      1 RDKRQARRGR RRAKWKTLLK KVLKAC
                          ====== ====
HITS AT:    15-24

REFERENCE   1:  138:70348

L9   ANSWER 23 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   478550-80-0  REGISTRY
CN   L-Cysteinamide, 2-aminododecanoylglycyl-L-cysteinyl-L-cysteinyl-L-
     seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-
     L-α-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl- (9CI)
     (CA INDEX NAME)
SQL  17

SEQ      1 XGCCSNPVCH LEHSNLC
              ======= ===
HITS AT:    4-13

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  138:338486

REFERENCE   2:  138:39520

L9   ANSWER 24 OF 61  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   478550-79-7  REGISTRY
CN   L-Cysteinamide, 2-aminododecanoylglycyl-L-cysteinyl-L-cysteinyl-L-
     seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-
     L-α-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-,
     cyclic (3→9),(4→17)-bis(disulfide) (9CI)  (CA INDEX
```

NAME)
SQL 17

SEQ 1 XGCCSNPVCH LEHSNLC
=======
HITS AT: 4-13

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:338486

REFERENCE 2: 138:39520

L9 ANSWER 25 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **427884-68-2** REGISTRY
CN L-Proline, L-methionyl-L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-prolyl-L-threonyl-L-prolyl-L-isoleucyl-L-glutaminyl-L-leucyl-L-asparaginyl-L-prolylglycyl-L-prolyl-L-leucyl-L-seryl-L-seryl-L-isoleucyl-L-phenylalanyl-L-seryl-L-arginyl-L-isoleucylglycyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
SQL 26

SEQ 1 MPKKKPTPIQ LNPGPLSSIF SRIGDP
=====
HITS AT: 16-25

REFERENCE 1: 136:382091

L9 ANSWER 26 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **427884-67-1** REGISTRY
CN L-Proline, L-prolyl-L-leucyl-L-seryl-L-seryl-L-isoleucyl-L-phenylalanyl-L-seryl-L-arginyl-L-isoleucylglycyl-L-α-aspartyl-L-prolylglycyl-L-methionyl-L-prolyl-L-lysyl-L-lysyl-L-lysyl-L-prolyl-L-threonyl-L-prolyl-L-isoleucyl-L-glutaminyl-L-leucyl-L-asparaginyl- (9CI) (CA INDEX NAME)
SQL 26

SEQ 1 PLSSIFSRIG DPGMPKKKPT PIQLNP
=========
HITS AT: 2-11

REFERENCE 1: 136:382091

L9 ANSWER 27 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **408501-56-4** REGISTRY
CN L-Glutamic acid, N-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)carbonyl]-β-alanyl-L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-norleucyl-L-lysyl-L-tryptophyl-L-lysyl-L-lysyl-L-prolyl-L-α-glutamylglycyl-L-α-aspartyl-O-phosphono-L-tyrosyl-L-α-glutamyl-L-α-glutamyl-L-valyl-L-leucyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 27

SEQ 1 XRQIKIWFQN RRXKWKKPEG DYEEVLE
======
HITS AT: 15-24

REFERENCE 1: 136:295079

L9 ANSWER 28 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **408494-98-4** REGISTRY
CN L-Glutamic acid, L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-norleucyl-L-lysyl-L-tryptophyl-L-lysyl-L-lysyl-L-prolyl-L-α-glutamylglycyl-L-α-aspartyl-O-phosphono-L-tyrosyl-L-α-glutamyl-L-α-glutamyl-L-valyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 26

SEQ 1 RQIKIWFQNR RXKWKKPEGD YEEVLE
=======
HITS AT: 14-23

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:295079

L9 ANSWER 29 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **408494-97-3** REGISTRY
CN L-Glutamic acid, L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-norleucyl-L-lysyl-L-tryptophyl-L-lysyl-L-lysyl-L-prolyl-L-α-glutamylglycyl-L-α-aspartyl-L-tyrosyl-L-α-glutamyl-L-α-glutamyl-L-valyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 26

SEQ 1 RQIKIWFQNR RXKWKKPEGD YEEVLE
=======
HITS AT: 14-23

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:295079

L9 ANSWER 30 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **267236-85-1** REGISTRY
CN L-Proline, L-prolyl-L-isoleucyl-L-seryl-L-seryl-L-isoleucyl-L-phenylalanyl-L-seryl-L-arginyl-L-isoleucylglycyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6: PN: WO0026379 FIGURE: 3 unclaimed sequence
SQL 12

SEQ 1 PISSIFSRIG DP
=========
HITS AT: 2-11

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:331146

L9 ANSWER 31 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **267007-59-0** REGISTRY

CN L-Proline, L-prolyl-L-leucyl-L-seryl-L-seryl-L-isoleucyl-L-phenylalanyl-L-seryl-L-arginyl-L-isoleucylglycyl-L-α-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 26: PN: WO0046376 PAGE: 2 unclaimed sequence
CN 284: PN: WO03018758 SEQID: 284 claimed sequence
CN 302: PN: WO03012068 SEQID: 302 unclaimed sequence
SQL 12

SEQ 1 PLSSIFSRIG DP
========= =
HITS AT: 2-11

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:226727

REFERENCE 2: 138:164688

REFERENCE 3: 133:173015

REFERENCE 4: 133:72618

REFERENCE 5: 132:331146

L9 ANSWER 32 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **267004-06-8** REGISTRY
CN β-Casein (cattle strain Korean isoform H fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AAD09813
CN GenBank AAD09813 (Translated from: GenBank AF104929)
CI MAN
SQL 40

SEQ 1 LEELNVPGEI VESLSSSEES ITRINKKIEK FQSEEQQQTE
==========
HITS AT: 21-30

REFERENCE 1: 132:319992

L9 ANSWER 33 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **264913-85-1** REGISTRY
CN Peptide YY (human), 13-L-proline-14-L-alanine- (9CI) (CA INDEX NAME)
CI MAN
SQL 36

SEQ 1 YPIKPEAPGE DAPAEELNRY YASLRHYLNL VTRQRY
==== ======
HITS AT: 17-26

REFERENCE 1: 135:87255

REFERENCE 2: 132:303579

L9 ANSWER 34 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **251538-77-9** REGISTRY

CN L-Alanine, L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-histidyl-L-lysyl-L-tryptophyl-L-lysyl-L-lysyl-L-isoleucylglycyl-L-α-glutamyl-L-histidyl-L-phenylalanyl-L-valyl-L-histidyl-L-valyl-L-asparaginyl-L-alanyl-L-threonyl-L-phenylalanyl-L-valyl-L-asparaginyl-L-valyl-L-lysyl-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 35

SEQ 1 RQIKIWFQNR RHKWKKIGEH FVHVNATFVN VKCVA
=======

HITS AT: 14-23

REFERENCE 1: 132:11258

L9 ANSWER 35 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **251538-76-8** REGISTRY
CN L-Alanine, L-arginyl-L-glutaminyl-L-isoleucyl-L-lysyl-L-isoleucyl-L-tryptophyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-arginyl-L-arginyl-L-histidyl-L-lysyl-L-tryptophyl-L-lysyl-L-lysyl-L-isoleucylglycyl-L-α-glutamyl-L-histidyl-L-tyrosyl-L-valyl-L-histidyl-L-valyl-L-asparaginyl-L-alanyl-L-threonyl-L-tyrosyl-L-valyl-L-asparaginyl-L-valyl-L-lysyl-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 35

SEQ 1 RQIKIWFQNR RHKWKKIGEH YVHVNATYVN VKCVA
=======

HITS AT: 14-23

REFERENCE 1: 132:11258

L9 ANSWER 36 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **229482-16-0** REGISTRY
CN L-Leucinamide, N-[[3,6-dihydroxy-3'-oxospiro[anthracene-9(10H),1'(3'H)-isobenzofuran]-5'(or 6')-yl]carbonyl]-L-leucyl-L-lysyl-L-threonyl-L-leucyl-L-threonyl-L-α-glutamyl-L-threonyl-L-leucyl-L-lysyl-L-α-glutamyl-L-leucyl-L-threonyl-L-lysyl-L-threonyl-L-leucyl-L-threonyl-L-α-glutamyl- (9CI) (CA INDEX NAME)
CI IDS
SQL 18

SEQ 1 LKTLTETLKE LTKTLTEL
==========

HITS AT: 1-17

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:82577

L9 ANSWER 37 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **229482-14-8** REGISTRY
CN L-Leucinamide, N-[[3,6-dihydroxy-3'-oxospiro[anthracene-9(10H),1'(3'H)-isobenzofuran]-5'(or 6')-yl]carbonyl]-L-leucyl-L-lysyl-L-threonyl-L-leucyl-L-alanyl-L-threonyl-L-alanyl-L-leucyl-L-

threonyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-threonyl-L-leucyl-L-threonyl-L-threonyl- (9CI) (CA INDEX NAME)
CI IDS
SQL 18

SEQ 1 LKTLATALTK LAKTLTTL
=== =======
HITS AT: 8-17

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 131:82577

L9 ANSWER 38 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **227199-94-2** REGISTRY
CN L-Arginine, L-tyrosyl-L-alanyl-L-arginyl-L-lysyl-L-alanyl-L-arginyl-L-arginyl-L-glutaminyl-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10: PN: WO03076561 SEQID: 10 claimed sequence
CN 13: PN: US20030190364 SEQID: 13 claimed sequence
CN 24: PN: WO0198324 SEQID: 27 claimed protein
CN 2: PN: WO02085305 PAGE: 68 claimed sequence
CN 2: PN: WO02088370 SEQID: 2 claimed protein
CN 36: PN: WO0062067 SEQID: 3 claimed sequence
CN 4: PN: WO03042239 PAGE: 28 claimed protein
CN 50: PN: US20030054000 SEQID: 3 claimed sequence
CN 76: PN: WO0183554 SEQID: 127 claimed protein
CN 8: PN: EP1342781 SEQID: 10 claimed protein
SQL 11

SEQ 1 YARKARRQAR R
========= =
HITS AT: 2-11

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:312392

REFERENCE 2: 139:256284

REFERENCE 3: 139:241319

REFERENCE 4: 139:2887

REFERENCE 5: 138:253701

REFERENCE 6: 138:215298

REFERENCE 7: 138:188077

REFERENCE 8: 137:364339

REFERENCE 9: 137:358059

REFERENCE 10: 136:64121

L9 ANSWER 39 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-56-6** REGISTRY

CN L-Threonine, L-valyl-L-threonyl-L-valyl-L-leucyl-L-alanyl-L-leucylglycyl-L-alanyl-L-leucyl-L-alanylglycyl-L-valylglycyl-L-valylglycyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 31

SEQ 1 VTVLALGALA GVGVGYKEAT STFTNITYRG T
===== =====

HITS AT: 16-25

REFERENCE 1: 129:260833

L9 ANSWER 40 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-50-0** REGISTRY
CN L-Threonine, (4R)-2-carboxy-4-thiazolidinecarbonyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl-, (1→16')-amide with L-valyl-L-threonyl-L-valyl-L-leucyl-L-alanyl-L-leucylglycyl-L-alanyl-L-leucyl-L-alanylglycyl-L-valylglycyl-L-valylglycyl-L-lysinamide (9CI) (CA INDEX NAME)
SQL 33,16,17

SEQ 1 VTVLALGALA GVGVGK

SEQ 1 PYKEATSTFT NITYRGT
========= =

HITS AT: 2-11

REFERENCE 1: 129:260833

L9 ANSWER 41 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-48-6** REGISTRY
CN L-Threonine, N2-(L-alanyl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-leucyl-L-prolyl-L-alanyl-L-valyl-L-leucyl-L-leucyl-L-alanyl-L-leucyl-L-leucyl-L-alanyl)-(4R)-2-(aminomethyl)-4-thiazolidinecarbonyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-prolyl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 32

SEQ 1 AAVALLPAVL LALLAXYKEA TPTFTNITYR GT
==== ======

HITS AT: 17-26

REFERENCE 1: 129:260833

L9 ANSWER 42 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-45-3** REGISTRY
CN L-Threonine, (4R)-2-carboxy-4-thiazolidinecarbonyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl-, (1→16')-amide with L-alanyl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-leucyl-L-prolyl-L-alanyl-L-valyl-L-leucyl-L-leucyl-L-alanyl-L-leucyl-L-leucyl-L-alanyl-L-lysinamide (9CI) (CA INDEX NAME)

SQL 33,16,17

SEQ 1 AAVALLPAVL LALLAK

SEQ 1 PYKEATSTFT NITYRGT
========= =
HITS AT: 2-11

REFERENCE 1: 129:260833

L9 ANSWER 43 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-42-0** REGISTRY
CN L-Threonine, N2-(L-alanyl-L-alanyl-L-valyl-L-alanyl-L-leucyl-L-leucyl-L-prolyl-L-alanyl-L-valyl-L-leucyl-L-leucyl-L-alanyl-L-leucyl-L-leucyl-L-alanyl)-(4R)-2-(aminomethyl)-4-thiazolidinecarbonyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 32

SEQ 1 AAVALLPAVL LALLAXYKEA TSTFTNITYR GT
==== ======
HITS AT: 17-26

REFERENCE 1: 129:260833

L9 ANSWER 44 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-31-7** REGISTRY
CN L-Threonine, L-cysteinyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-prolyl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 CYKEATPTFT NITYRGT
========= =
HITS AT: 2-11

REFERENCE 1: 129:260833

L9 ANSWER 45 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **213546-28-2** REGISTRY
CN L-Threonine, L-cysteinyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 CYKEATSTFT NITYRGT
========= =
HITS AT: 2-11

REFERENCE 1: 129:260833

L9 ANSWER 46 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **206770-27-6** REGISTRY
CN L-Threonine, L-histidyl-L-α-aspartyl-L-arginyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-alanyl-L-lysyl-L-phenylalanyl-L-

α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-arginyl-L-alanyl-L-arginyl-L-alanyl-L-lysyl-L-tryptophyl-L-α-aspartyl-L-threonyl-L-alanyl-L-asparaginyl-L-asparaginyl-L-prolyl-L-lysyl-L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 41

SEQ 1 HDRKEFAKFE EERARAKWDT ANNPKYKEAT STFTNITYRG T
                                    ===== =====

HITS AT: 26-35

REFERENCE 1: 128:304071

L9 ANSWER 47 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **206748-54-1** REGISTRY
CN L-Lysine, L-valyl-L-threonyl-L-valyl-L-leucyl-L-alanyl-L-leucylglycyl-L-alanyl-L-leucyl-L-alanylglycyl-L-valylglycyl-L-valylglycyl-L-tyrosyl-L-lysyl-L-seryl-L-alanyl-L-valyl-L-threonyl-L-threonyl-L-valyl-L-valyl-L-asparaginyl-L-prolyl-L-lysyl-L-tyrosyl-L-α-glutamylglycyl- (9CI) (CA INDEX NAME)
SQL 31

SEQ 1 VTVLALGALA GVGVGYKSAV TTVVNPKYEG K
                        ===== =====

HITS AT: 16-25

REFERENCE 1: 128:304071

L9 ANSWER 48 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **206748-53-0** REGISTRY
CN L-Lysine, L-tyrosyl-L-lysyl-L-seryl-L-alanyl-L-valyl-L-threonyl-L-threonyl-L-valyl-L-valyl-L-asparaginyl-L-prolyl-L-lysyl-L-tyrosyl-L-α-glutamylglycyl- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 YKSAVTTVVN PKYEGK
      ==========

HITS AT: 1-10

REFERENCE 1: 128:304071

L9 ANSWER 49 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **203065-48-9** REGISTRY
CN L-Lysine, L-lysyl-L-glutaminyl-L-α-glutamyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-alanyl-L-tyrosyl-L-glutaminyl-L-lysyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)
SQL 17

SEQ 1 KQEAKLAAKE AYQKLLK
          === =======

HITS AT: 8-17

REFERENCE 1: 128:162866

L9 ANSWER 50 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN

RN **196216-55-4** REGISTRY
CN L-Serine, N2-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-L-arginyl-L-arginyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-arginyl-L-arginyl-L-prolyl-L-valyl-L-prolyl-L-α-glutamyl-O-phosphono-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-glutaminyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 30

SEQ 1 XXXXXRRWRR WWRRWWRRWR RPVPEYINQS
=== ========== ========
HITS AT: 8-28

REFERENCE 1: 127:257993

L9 ANSWER 51 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **189036-95-1** REGISTRY
CN L-Arginine, L-arginyl-L-arginyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-tryptophyl-L-arginyl-L-arginyl-L-tryptophyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 16: PN: WO02088370 SEQID: 17 claimed protein
CN 4: PN: WO03004600 SEQID: 4 claimed protein
SQL 16

SEQ 1 RRWRRWWRRW WRRWRR
======== ======
HITS AT: 3-16

REFERENCE 1: 138:103296

REFERENCE 2: 137:364339

REFERENCE 3: 126:273944

L9 ANSWER 52 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **188425-81-2** REGISTRY
CN L-Glutamic acid, N-(1-oxooctadecyl)-L-tyrosyl-L-α-glutamyl-L-threonyl-L-leucyl-L-leucyl-L-isoleucyl-L-α-glutamyl-L-threonyl-L-alanyl-L-seryl-L-seryl-L-leucyl-L-valyl-L-lysyl-L-asparaginyl-L-alanyl-L-isoleucyl-L-glutaminyl-L-leucyl-L-seryl-L-isoleucyl- (9CI) (CA INDEX NAME)
SQL 22

SEQ 1 YETLLIETAS SLVKNAIQLS IE
== ========
HITS AT: 9-18

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:54904

REFERENCE 2: 132:9287

REFERENCE 3: 126:233779

L9 ANSWER 53 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **188425-80-1** REGISTRY
CN L-Tyrosine, N-(1-oxooctadecyl)-L-α-aspartyl-L-leucyl-L-isoleucyl-L-α-glutamyl-L-α-glutamyl-L-alanyl-L-alanyl-L-seryl-L-arginyl-L-isoleucyl-L-valyl-L-α-aspartyl-L-alanyl-L-valyl-L-isoleucyl-L-α-glutamyl-L-glutaminyl-L-valyl-L-lysyl-L-alanyl-L-alanylglycyl-L-alanyl- (9CI) (CA INDEX NAME)
SQL 24

SEQ 1 DLIEEAASRI VDAVIEQVKA AGAY
========= ==
HITS AT: 3-12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 132:54904

REFERENCE 2: 132:9287

REFERENCE 3: 126:233779

L9 ANSWER 54 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **186420-62-2** REGISTRY
CN α-Conotoxin M II (reduced) (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 GCCSNPVCHL EHSNLC
========= ==
HITS AT: 3-12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:338486

REFERENCE 2: 138:39520

REFERENCE 3: 126:182612

REFERENCE 4: 126:152786

REFERENCE 5: 126:126900

L9 ANSWER 55 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **185529-64-0** REGISTRY
CN Pandinotoxin Kα (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Arginine, L-threonyl-L-isoleucyl-L-seryl-L-cysteinyl-L-threonyl-L-asparaginyl-L-prolyl-L-lysyl-L-glutaminyl-L-cysteinyl-L-tyrosyl-L-prolyl-L-histidyl-L-cysteinyl-L-lysyl-L-lysyl-L-α-glutamyl-L-threonylglycyl-L-tyrosyl-L-prolyl-L-asparaginyl-L-alanyl-L-lysyl-L-cysteinyl-L-methionyl-L-asparaginyl-L-arginyl-L-lysyl-L-cysteinyl-L-lysyl-L-cysteinyl-L-phenylalanylglycyl-, cyclic (4→25),(10→30),(14→32)-tris(disulfide)
CN Pandinustoxin Kα
CN Toxin Pi 2 (Pandinus imperator)
CI MAN
SQL 35

SEQ 1 TISCTNPKQC YPHCKKETGY PNAKCMNRKC KCFGR
==== ======
HITS AT: 7-16

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:15325

REFERENCE 2: 132:319525

REFERENCE 3: 132:275345

REFERENCE 4: 131:126593

REFERENCE 5: 127:230516

REFERENCE 6: 126:140774

REFERENCE 7: 126:85890

L9 ANSWER 56 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **182752-56-3** REGISTRY
CN L-Threonine, L-tyrosyl-L-lysyl-L-α-glutamyl-L-alanyl-L-threonyl-L-seryl-L-threonyl-L-phenylalanyl-L-threonyl-L-asparaginyl-L-isoleucyl-L-threonyl-L-tyrosyl-L-arginylglycyl- (9CI) (CA INDEX NAME)
SQL 16

SEQ 1 YKEATSTFTN ITYRGT
==========
HITS AT: 1-10

REFERENCE 1: 135:29423

REFERENCE 2: 128:304071

REFERENCE 3: 125:268630

L9 ANSWER 57 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **175735-93-0** REGISTRY
CN α-Conotoxin M II (9CI) (CA INDEX NAME)
OTHER NAMES:
CN L-Cysteinamide, glycyl-L-cysteinyl-L-cysteinyl-L-seryl-L-asparaginyl-L-prolyl-L-valyl-L-cysteinyl-L-histidyl-L-leucyl-L-α-glutamyl-L-histidyl-L-seryl-L-asparaginyl-L-leucyl-, cyclic (2→8),(3→16)-bis(disulfide)
SQL 16

SEQ 1 GCCSNPVCHL EHSNLC
======== ==
HITS AT: 3-12

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:302174

REFERENCE 2: 139:240692

REFERENCE 3: 139:95698

REFERENCE 4: 138:338486

REFERENCE 5: 138:131468

REFERENCE 6: 138:117865

REFERENCE 7: 138:39520

REFERENCE 8: 138:540

REFERENCE 9: 137:273401

REFERENCE 10: 137:226853

L9 ANSWER 58 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **162261-10-1** REGISTRY
CN 1-45-Defensin, pro- (human clone HNP-1 reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 20-64-Defensin, prepro- (human clone HNP-1 reduced)
CI MAN
SQL 45

SEQ 1 EPLQARADEV AAAPEQIAAD IPEVVVSLAW DESLAPKHPG SRKNM
======= ===

HITS AT: 14-23

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 124:314980

REFERENCE 2: 122:233688

L9 ANSWER 59 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **153421-75-1** REGISTRY
CN L-Serine, L-lysyl-L-alanyl-L-leucyl-L-isoleucyl-L-histidyl-L-leucyl-L-seryl-L-α-aspartyl-L-leucyl-L-arginyl-L-α-glutamyl-L-tyrosyl-L-arginyl-L-arginyl-L-phenylalanyl-L-α-glutamyl-L-lysyl-L-α-glutamyl-L-lysyl-L-leucyl-L-lysyl-L-seryl-L-glutaminyl-L-tryptophyl-L-asparaginyl-L-asparaginyl-L-α-aspartyl-L-asparaginyl-L-prolyl-L-leucyl-L-phenylalanyl-L-lysyl-L-seryl-L-alanyl-L-threonyl-L-threonyl-L-threonyl-L-valyl-L-methionyl-L-asparaginyl-L-prolyl-L-lysyl-L-phenylalanyl-L-alanyl-L-α-glutamyl- (9CI) (CA INDEX NAME)
CI MAN
SQL 46

SEQ 1 KALIHLSDLR EYRRFEKEKL KSQWNNDNPL FKSATTTVMN PKFAES
========== ======

HITS AT: 31-40

REFERENCE 1: 128:304071

REFERENCE 2: 120:159885

L9 ANSWER 60 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **118997-30-1** REGISTRY
CN Peptide YY (human) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Neuropeptide Y (pig), 3-L-isoleucine-6-L-glutamic acid-7-L-alanine-13-L-serine-14-L-proline-16-L-glutamic acid-18-L-asparagine-22-L-alanine-23-L-serine-28-L-leucine-31-L-valine-
OTHER NAMES:
CN Human peptide YY
CN L-Tyrosinamide, L-tyrosyl-L-prolyl-L-isoleucyl-L-lysyl-L-prolyl-L-α-glutamyl-L-alanyl-L-prolylglycyl-L-α-glutamyl-L-α-aspartyl-L-alanyl-L-seryl-L-prolyl-L-α-glutamyl-L-α-glutamyl-L-leucyl-L-asparaginyl-L-arginyl-L-tyrosyl-L-tyrosyl-L-alanyl-L-seryl-L-leucyl-L-arginyl-L-histidyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-leucyl-L-valyl-L-threonyl-L-arginyl-L-glutaminyl-L-arginyl-
CI MAN
SQL 36

SEQ 1 YPIKPEAPGE DASPEELNRY YASLRHYLNL VTRQRY
==== ======
HITS AT: 17-26

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:79376

REFERENCE 2: 136:397946

REFERENCE 3: 136:289341

REFERENCE 4: 136:161700

REFERENCE 5: 136:32130

REFERENCE 6: 135:17912

REFERENCE 7: 134:348357

REFERENCE 8: 134:336414

REFERENCE 9: 134:173145

REFERENCE 10: 133:38647

L9 ANSWER 61 OF 61 REGISTRY COPYRIGHT 2003 ACS on STN
RN **107452-89-1** REGISTRY
CN ω-Conotoxin M VIIA (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 18,19,65,66,81,82-Hexathia-3,6,9,12,15,22,25,28,31,34,37,40,43,46,49,52,55,58,61,70,73,76,79,84-tetracosaazatricyclo[40.37.4.221,68]pentaoctacontane, cyclic peptide deriv.
OTHER NAMES:
CN ω-Conopeptide MVIIA (Conus)
CN ω-Conotoxin M VIIA (reduced), cyclic (1→16),(8→20),(15→25)-tris(disulfide)
CN Omega conopeptide MVIIA (Conus)

```
CN   SNX 111
CN   Ziconotide
SQL  25

SEQ      1 CKGKGAKCSR LMYDCCTGSC RSGKC
                   === =======
HITS AT:   8-17

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

REFERENCE   1:  139:224219

REFERENCE   2:  139:175022

REFERENCE   3:  139:159839

REFERENCE   4:  139:112996

REFERENCE   5:  139:63195

REFERENCE   6:  139:63155

REFERENCE   7:  138:343864

REFERENCE   8:  138:314620

REFERENCE   9:  138:282655

REFERENCE  10:  138:281004

     (FILE 'REGISTRY' ENTERED AT 11:30:32 ON 07 NOV 2003)
L10           44 S PLSSIFSRIGDP/SQSP

     FILE 'HCAPLUS' ENTERED AT 11:31:58 ON 07 NOV 2003
L11           29 S L10
L12            4 S L11 AND (CPP OR CELL PERMEAB?)

L13            0 L12 NOT L4

=> fil hom
FILE 'HOME' ENTERED AT 11:32:39 ON 07 NOV 2003
```

Seq. ID 2